

# Kyowa Hakko Bio's fermentation technology

## What is fermentation technology?

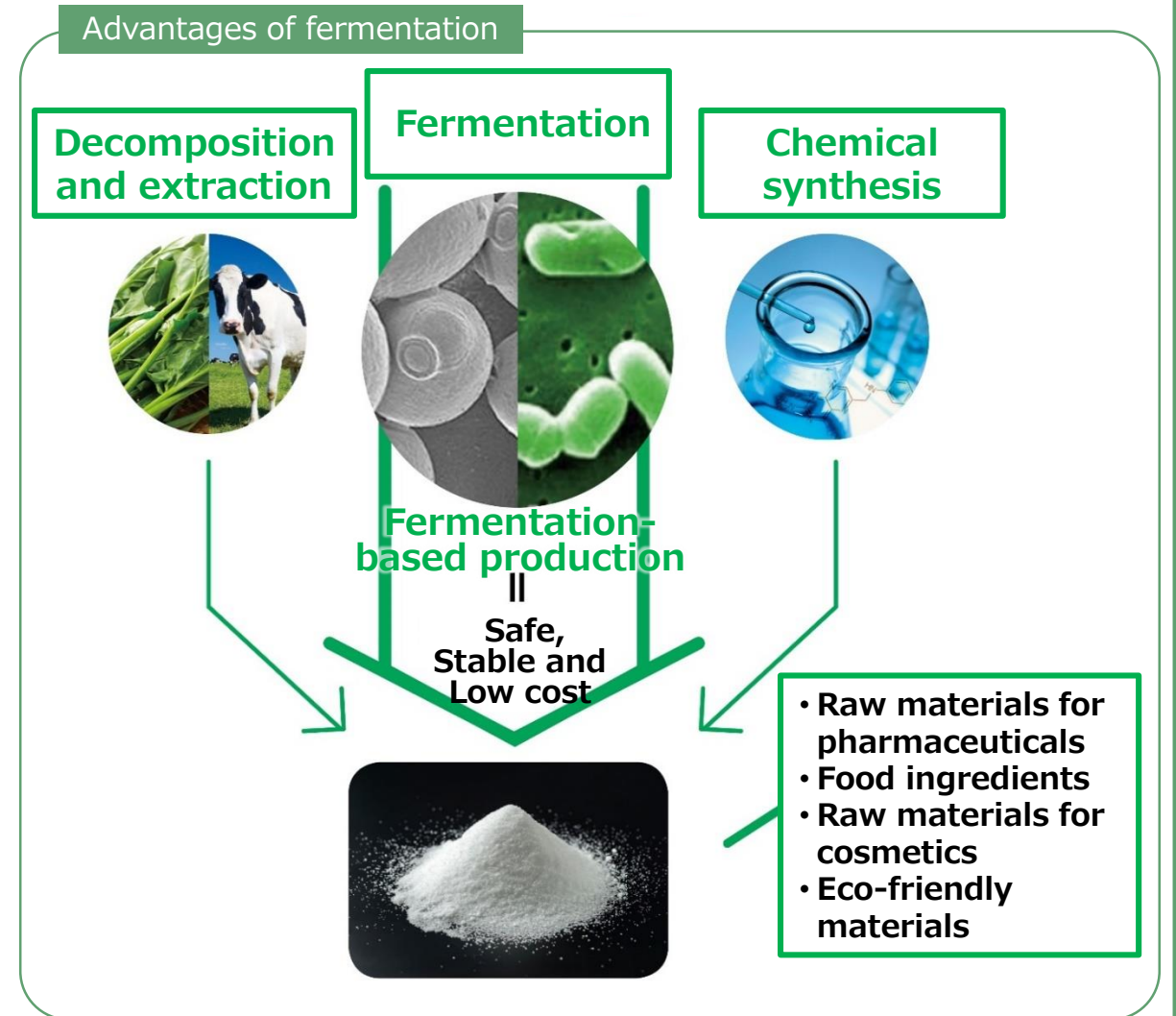
- Consists of having microorganisms produce amino acids and other valuable compounds, and then extracting these at a high level of purity

## Advantages of fermentation technology

- Fermentation technology enables the safe, stable and low-cost (mass) production of valuable compounds.



- Chemical synthesis involves the use of hazardous substances and carries risks to the environment
- Extraction from plant and animal sources may undermine sustainable food supply amidst warnings of food crises due to global population growth

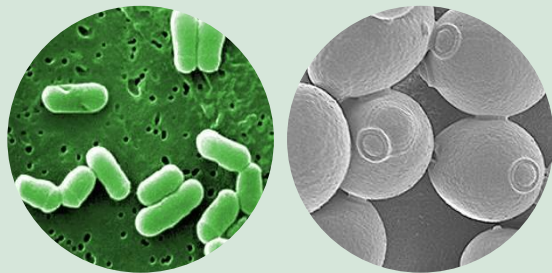


# Kyowa Hakko Bio's core technologies

All three technologies (Microbial breeding technology, industrialization technology and environmental technology) are necessary for fermentation-based production. Kyowa Hakko Bio has been refining and accumulating these technologies over the years.

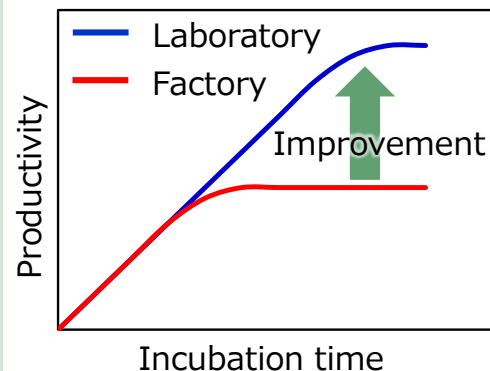
## Microbial breeding technology

Technology to create microorganisms that produce the desired ingredients



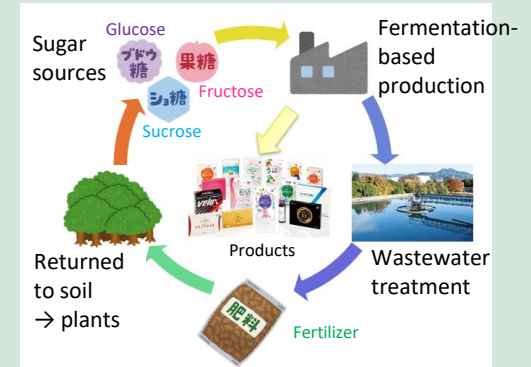
## Industrialization technology

Technology to realize safe, secure, and large-scale production



## Environmental technology

Technology for reducing environmental impact and processing liquid waste



## Microbial breeding technology

Technical issue: creating microorganisms capable of producing compounds on an industrial scale is difficult

Technological capabilities for solving this issue: we possess know-how on microbial breeding that enables establishing production systems and can be used for a variety of compounds

### Design

Metabolic control technology developed over many years

- Design of metabolic pathways for microorganisms

Hypothesis formulation  
Improvement plan

### On-site installation testing

- Cause analysis and analysis of gap between small- and large-volume cultures

### Breeding

Use of findings from previous studies

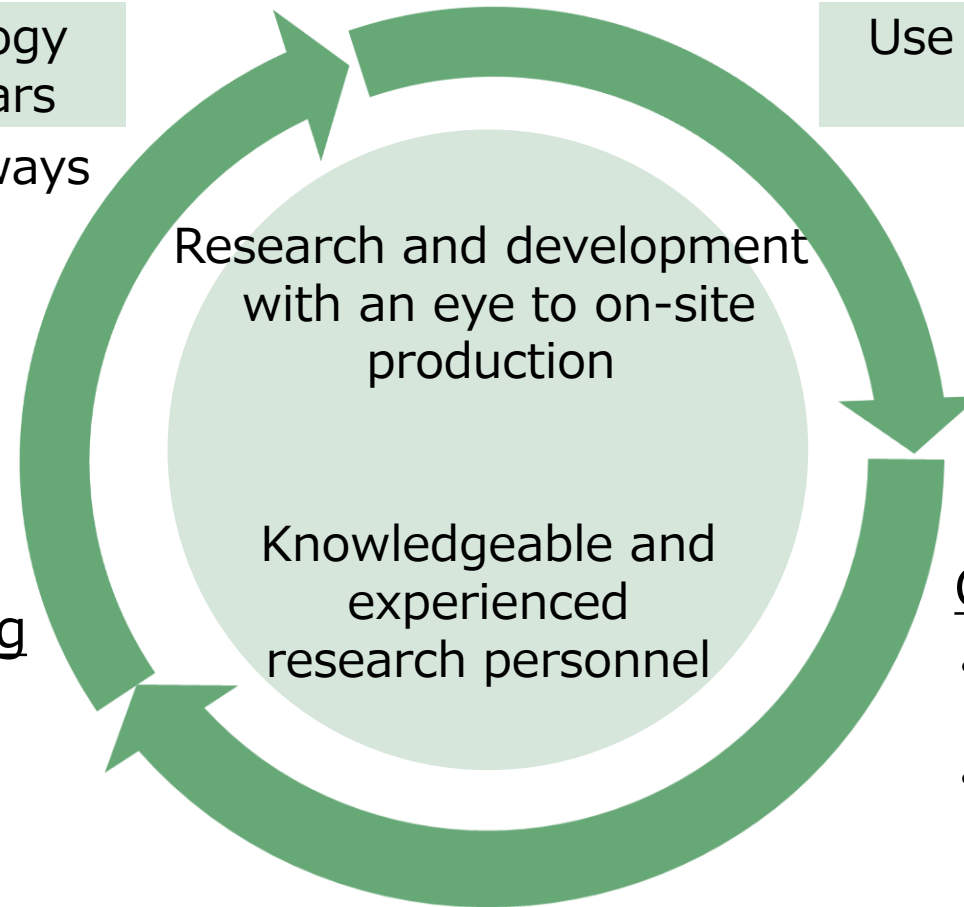
- Genetic design
- Enzyme modification
- Transgenesis

### Culture and analysis

- Optimization of microbial culture
- Measurement of products and byproducts

Research and development with an eye to on-site production

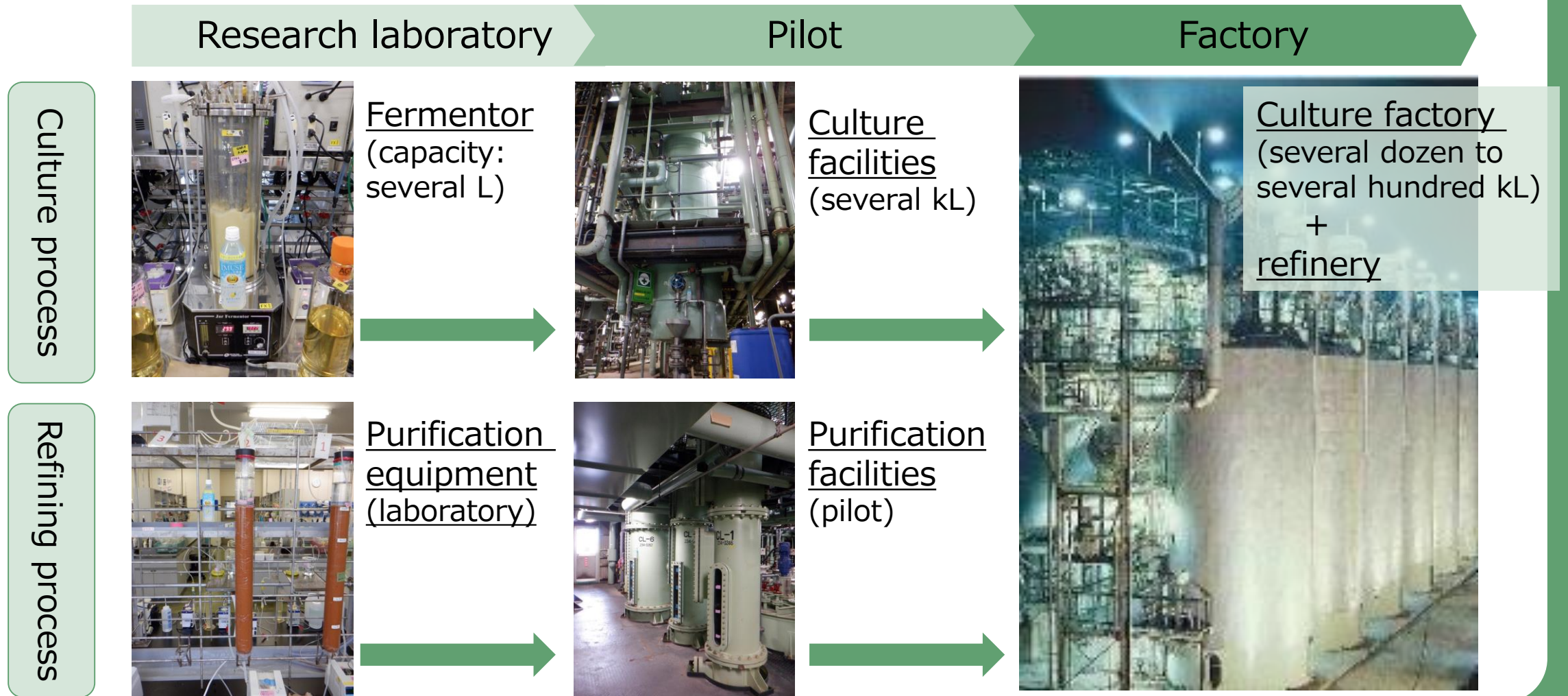
Knowledgeable and experienced research personnel



# Industrialization technology

Technical issue: stable production becomes more difficult as cultures grow in size

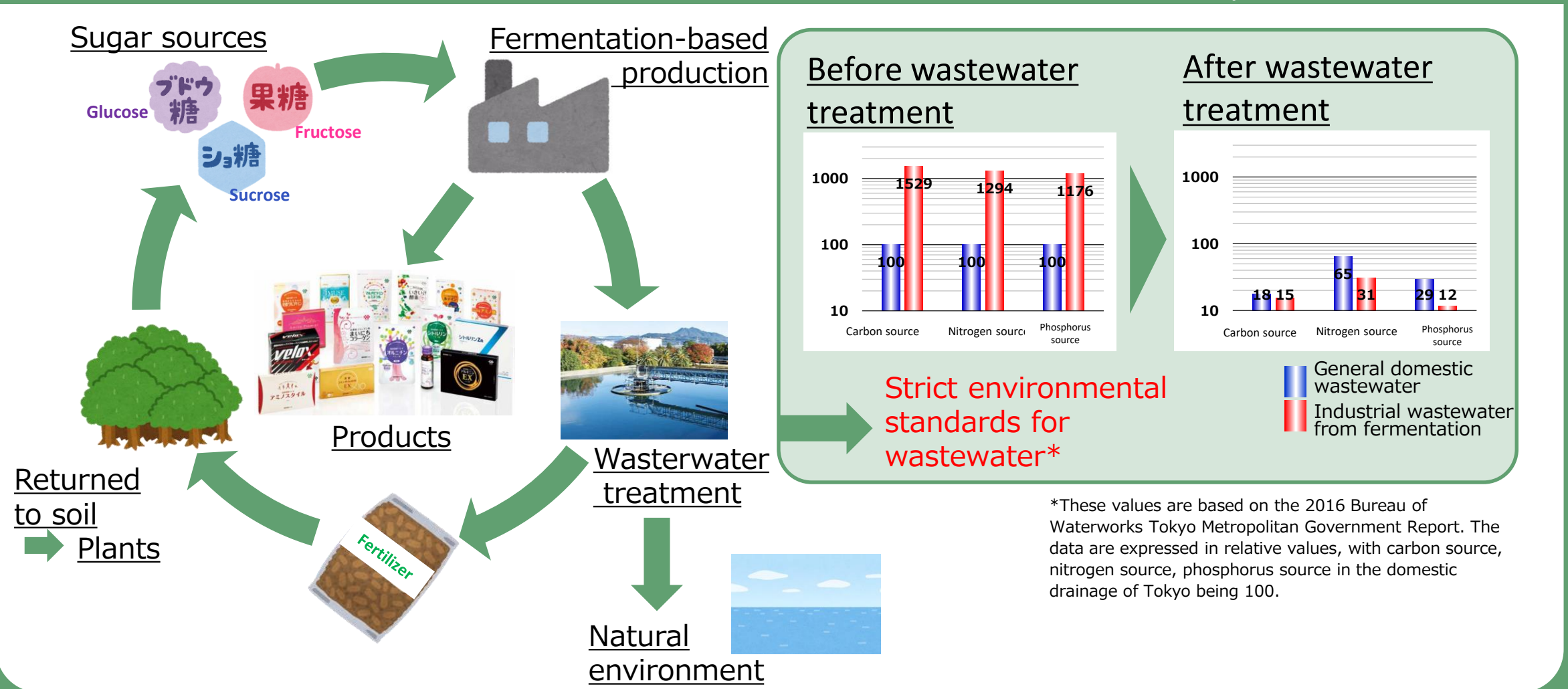
Technological capabilities for solving this issue: industrial-scale manufacturing achieved through technical verification with pilot facilities



# Environmental technology

Technical issue: industrial production is not possible without efficient treatment technology for the waste liquids from fermentation

Technological capabilities for solving this issue: develop a highly efficient treatment process for industrial wastewater from fermentation in order to reduce the environmental impact



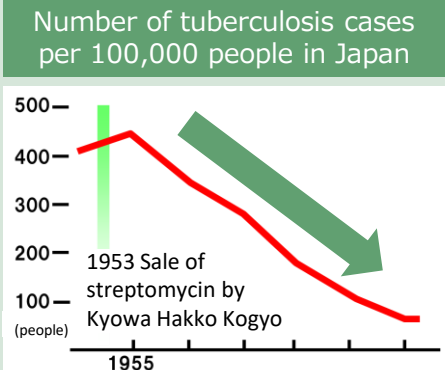
# A history of creating and accumulating technologies

We have been pioneers in creating new technologies, aiming to use fermentation technology to solve the social issues

1951 1956 1958 1993 1998 2000 2004

## Helped eradicate tuberculosis

- Introduced technology for the production of streptomycin, a tuberculosis drug, to Japan in order to help reduce the number of tuberculosis cases



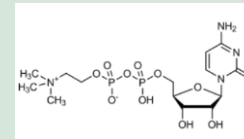
## Developed the world's first fermentation-based technology for the production of amino acids

- **L-Glutamine**  
Revolutionized the seasoning industry
- **L-Lysine**  
A breakthrough in the history of livestock feed



➔ First corporate recipient of the **Japan Academy Prize**

## Developed technology for the bio-production of citicoline, a drug for the treatment of impaired consciousness

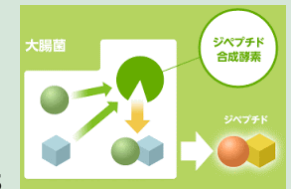


## First in the world to develop oligosaccharide production technology



## Developed dipeptide fermentation technology and established a production system

- Contributing to nutritional support for the sick through use in infusions



## World's first successful production of human milk oligosaccharides by microorganisms

- Mass production technology to provide infants with powdered milk that is similar to breast milk, and adults with the health benefits of breast milk



# Kyowa Hakko Bio's research and development system

## Basic research (R&I Center)

- Develops new production processes using **microbial breeding technology**

## Research on industrialization (Technical Research Laboratories)

- Uses **microbial breeding technology, industrialization technology and environmental technology** to create robust processes that enable actual production

## Basic R&D data

- R&D expenses: 2.4 billion yen (in 2019)
- Researchers: 126 (as of April 2020)
- Number of patents (production process/crystallization): 119

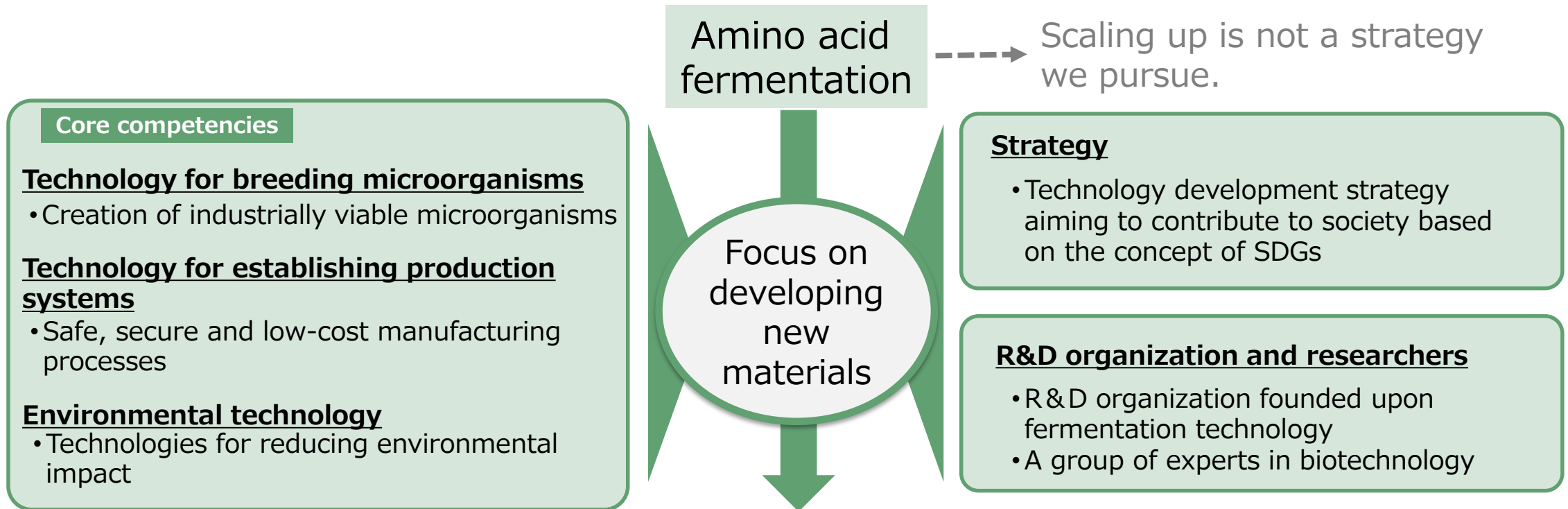


▲ R&I Center\* (Tsukuba City, Ibaraki Prefecture)  
\*Integrated into Kirin Holding's Kirin Central Research Institute, effective July 1, 2020.



▲ Technical Research Laboratories (Hofu City, Yamaguchi Prefecture)

Fermentation technology, the source of our competitive advantage, contributes to a sustainable society  
As a result of continuously channeling R&D resources into the development of new materials using amino acid fermentation technology rather than the expansion of amino acid production, we have been able to introduce technically challenging, high value-added materials to the market.



Development of high value-added functional materials and entry into new areas of biotechnology

Research on citicoline, human milk oligosaccharides(HMO), dipeptides and gut bacteria